Introduction

Influenza Vaccine Session

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Advisory Committee on Immunization Practices

June 28, 2007

CDC

Agenda: Influenza Session*

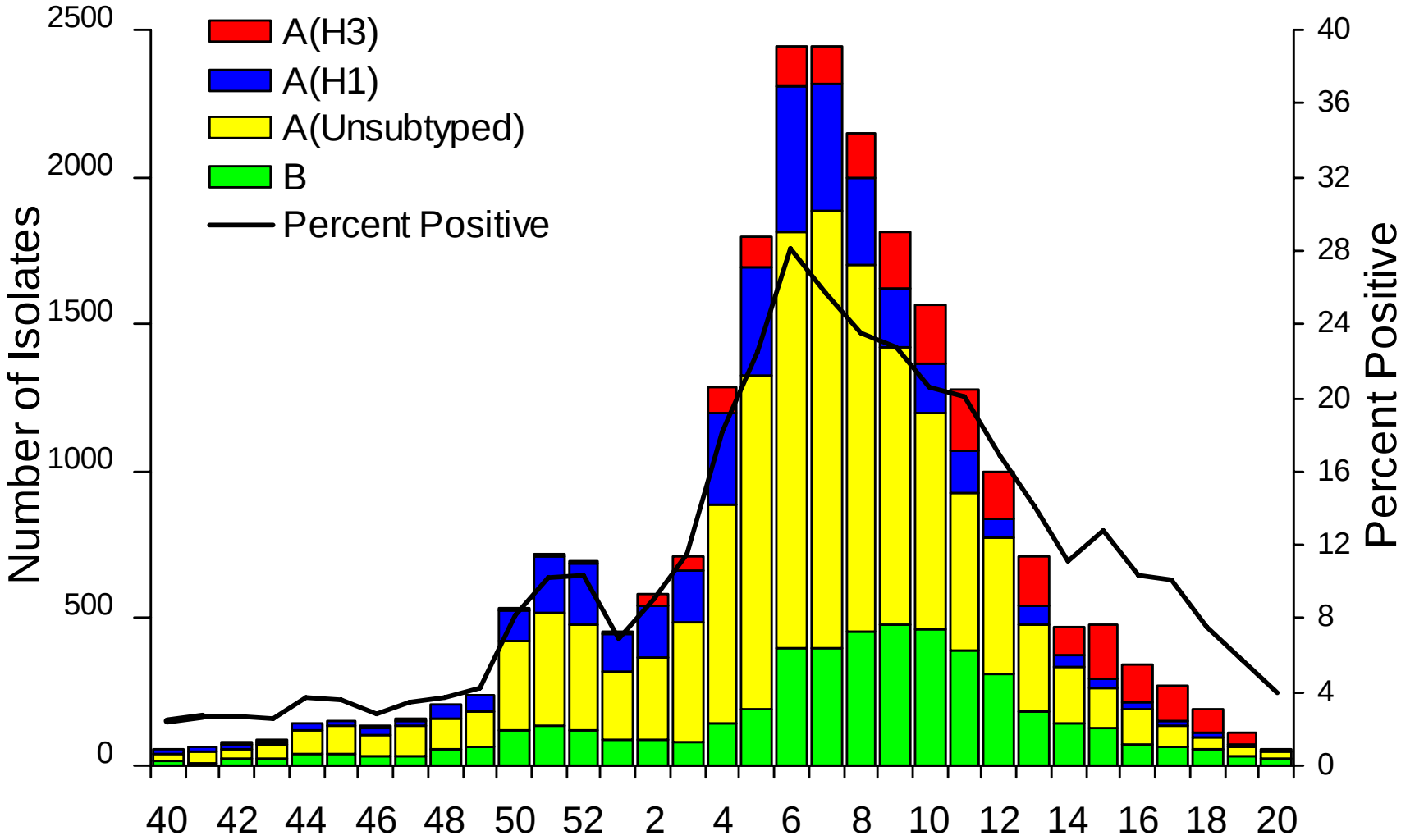
- Influenza activity in the US during 2006-2007
- September 2007 CDC-CSTE consultation: expanding recommendations to school age children
- Update: Licensure status for LAIV (FluMist, MedImmune) among young children
- Safety monitoring update – LAIV (*Karen Broder, Immunization Safety Office, CDC*)
- National Influenza Vaccine Summit (*Gina Mootrey, Immunization Services Division, CDC*)

***Vote on LAIV use for young children cancelled**

Influenza Activity in the United States, 2006-2007*

*Influenza Division, CDC Preliminary data

Number* and percentage of respiratory specimens testing positive for influenza reported by the World Health Organization and the National Respiratory and Enteric Virus Surveillance System collaborating laboratories, by week and year– United States, 2006-07 influenza season†



*N=175,514

† As of June 5, 2007

Percentage of visits for influenza-like illness (ILI) reported by the Sentinel Provider Surveillance Network, by week – United States, 2004-05, 2005-06, and 2006-07 influenza seasons

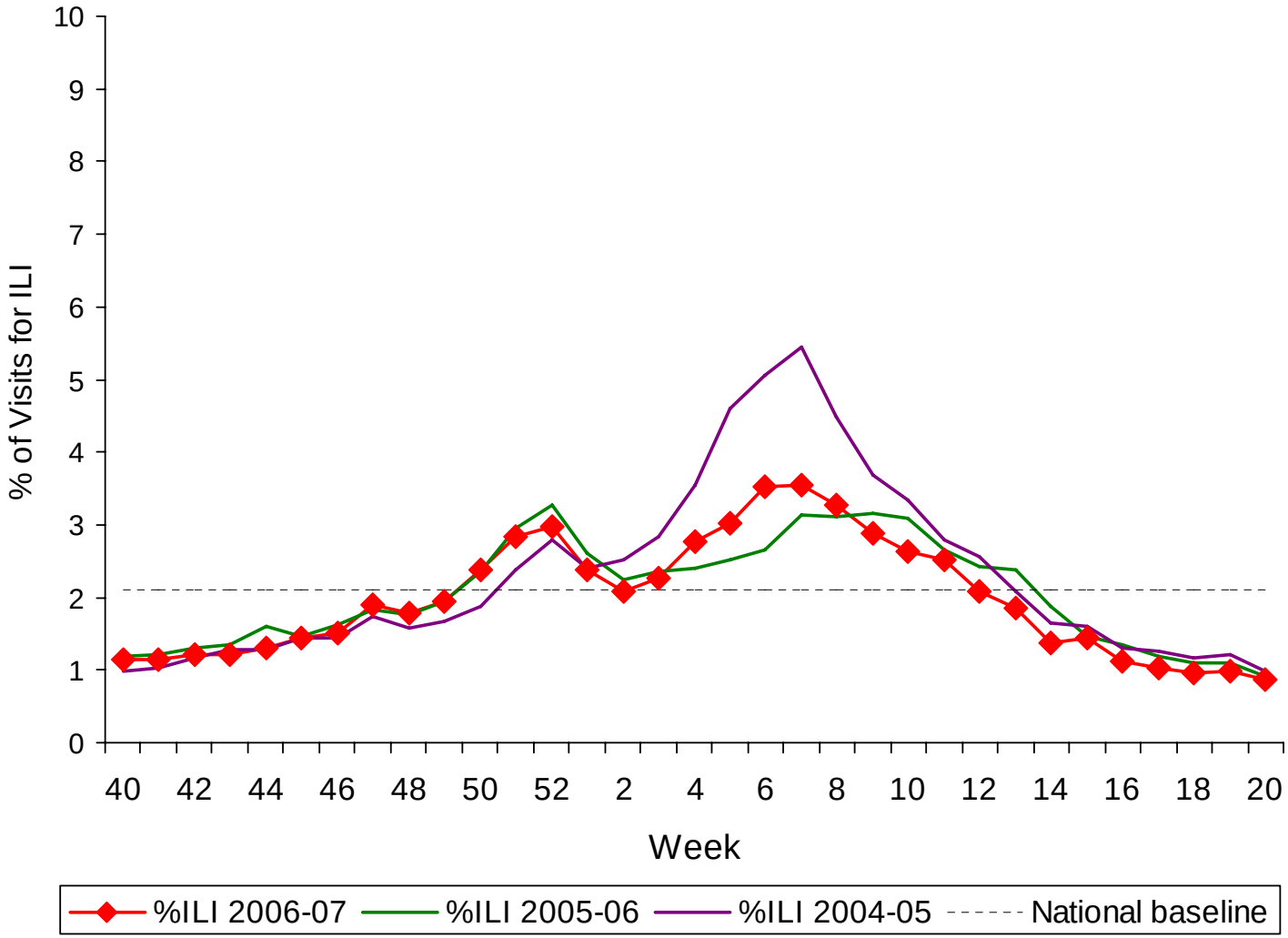
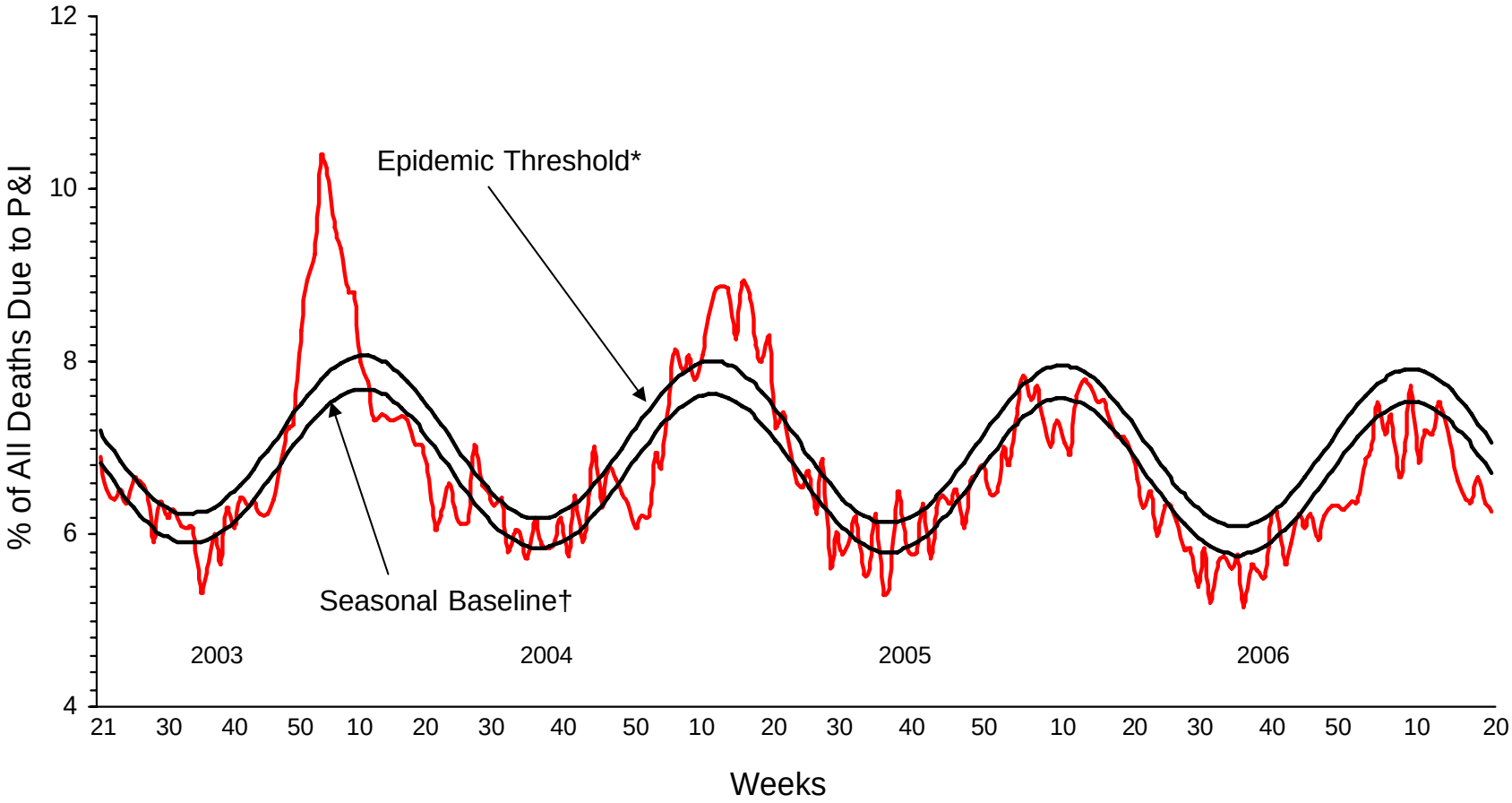
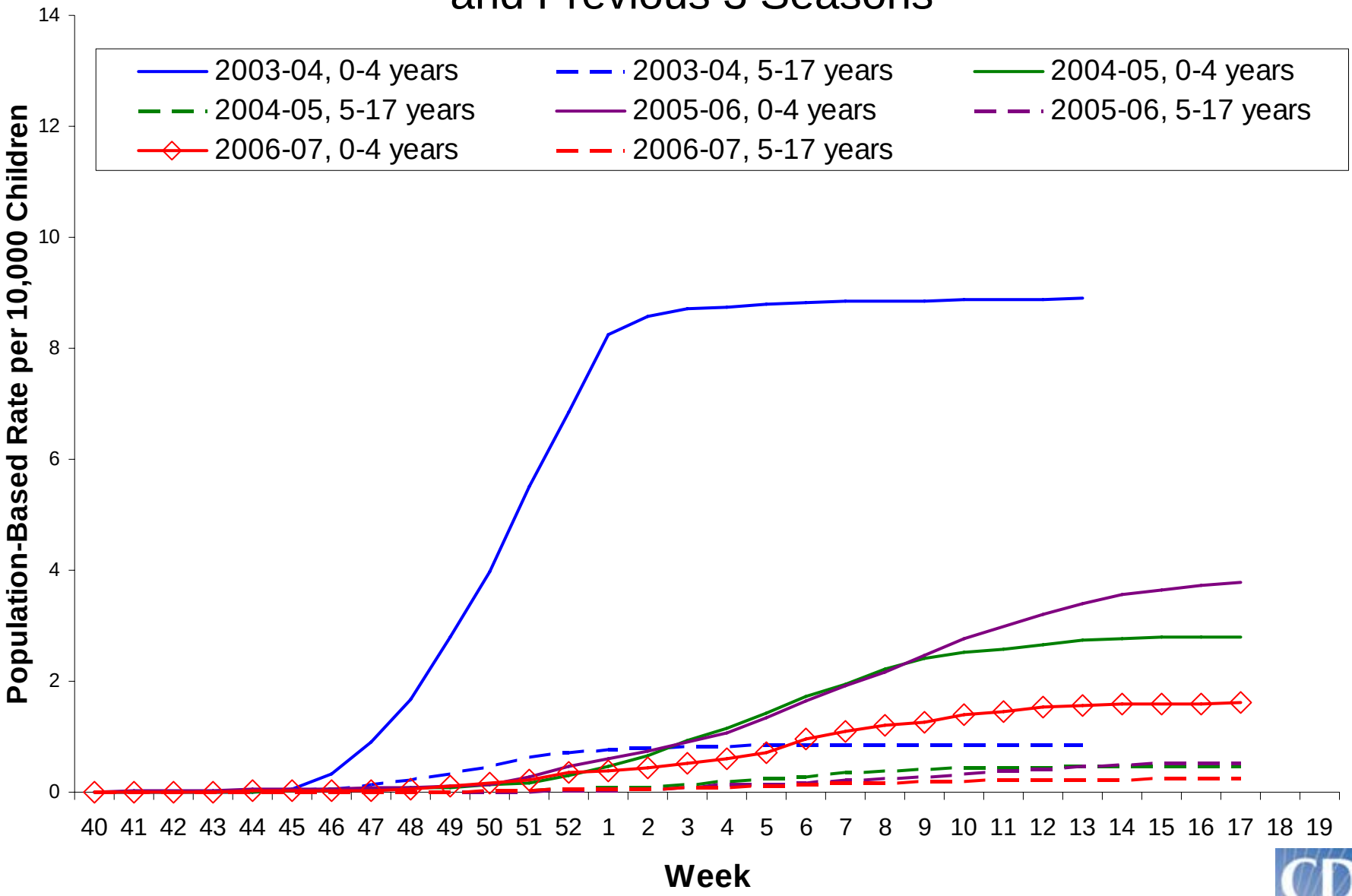


Figure 3. Percentage of deaths attributed to pneumonia and influenza (P&I) reported by the 122 Cities Mortality Reporting System, by week and year, 2003-2007



EIP Influenza Laboratory-Confirmed Cumulative Hospitalization Rates for Children Aged 0-4 and 5-17 years, 2006-07 and Previous 3 Seasons



Surveillance for Pediatric Deaths Attributed to Influenza Complications

- As of June 22, 2007, CDC has received 67 reports of influenza-associated pediatric deaths this influenza season (2006-2007)
  - 2005-2006: 45 deaths
  - 2004-2005: 46 deaths
  - 2003-2004: 153 deaths
- Compared to previous 2 seasons
  - Increase in mean age to 7 years (from 4-5 years in 2004-2006)*
  - Increase in proportion with invasive MRSA-associated co-infection from <5% to 27%*
    - Planning additional investigations and increased surveillance during upcoming season for MRSA-influenza co-infections among children

*preliminary data L Finelli, R Dhara, CDC

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Potential Time-Frame for Modifying Influenza Vaccination Recommendations

- **2007-2008**: Consider expanding recommendations to include school-age children
- **2010-2011**: Consider expansion of recommendations to include household contacts and caregivers of school-aged children
- **2012-2013**: Consider expansion to universal vaccination

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Expanding Recommendations to Include School-age Children

- CDC-CSTE sponsored consultation to consider scientific and implementation issues
  - September 10-11, 2007 in Atlanta
  - Approximately 75 consultants
    - Influenza researchers and epidemiologists
    - Public health and professional organization representatives
    - Community vaccinators
    - Safety experts
  - Mix of data presentations and small workgroups

- Outcome: Summarize evidence and address critical issues for presentation to the October 2007 ACIP meeting

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Expanding Influenza Vaccine Recommendations to School Age Children
September 2007 meeting objectives and topics

- **Review the evidence base supporting expansion of recommendations**
  - Burden of disease
  - Vaccine effectiveness and safety
  - Cost analyses
  - Potential direct and indirect impact
  - Experiences in pilot projects
- **Identify key evidence gaps**
- **Discuss implementation challenges and potential solutions**
  - Sustainability
  - Infrastructure and resource needs
  - Feasibility of delivering vaccine in non-medical settings
  - Priority communication messages
  - Impact assessment studies

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Vaccine Strain Recommendations, 2007-2008*

- an A/Solomon Islands/3/2006 (H1N1)-like virus (new strain);
- an A/Wisconsin/67/2005 (H3N2)-like virus (no change);
- a B/Malaysia/2506/2004-like virus (no change)

***Vaccines and Related Biologicals Advisory Board, FDA, February 28, 2007**

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FluMist Licensure History

- **June 2003**: FluMist (frozen) licensed for use in healthy persons aged 5-49 years

- **January 2007**: FluMist liquid formulation licensed to replace frozen formulation (first commercial use anticipated during 2007/08 influenza season)

- **May 2007:** FDA Vaccine and Related Product Biologics Advisory Committee (VRPBAC) reviewed MedImmune's Biologics License Application supplement for use of FluMist (liquid) in children aged 12-59 months without a history of wheeze/asthma

Update on Proposed FluMist Licensure Change

- May 16, 2007: MedImmune and FDA presented analyses to VRBPAC
- BLA supplement requested by MedImmune:
  - Children aged 12-59 months w/o history of wheezing and asthma
  - Primary data source: Pivotal trial CP111, published as Belshe et al, N Engl J Med, 2007*
    - Randomized double blind, active control (TIV) multicenter study
    - Pre-specified analyses for 6-23 months olds and 24-59 month olds

***Presented to ACIP in October 2006 and February 2007**

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Summary Findings from FDA Clinical Reviewer Analyses, CP111*

- FluMist is safe and effective in subjects 24 months of age and older
- Among subjects <24 months of age, participants who received FluMist had:
  - Increased hospitalizations
  - Increased severity of wheezing
  - Increased severity of respiratory events
- History of wheezing was poorly predictive of wheezing post-vaccination among FluMist recipients
- Post hoc analyses conducted among 6-11 month olds should be interpreted with caution

***T Cvetkovich, M Baylor and S Ahnn, VRBPAC presentations, May 16, 2007**

Available at: http://www.fda.gov/ohrms/dockets/ac/07/slides/2007-4292S1-0-index.html

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VRBPAC Recommendations, Supplement to FluMist BLA, May 16, 2007

- **Question 1: Do the data demonstrate the efficacy of FluMist for prevention of influenza in young children**
  - **All 15 voting members indicated efficacy demonstrated for children 6 months and older**
- **Question 2: Do the data demonstrate that the benefits will exceed the risk of FluMist® for use in**
  - The applicant's proposed population (children 12 to 59 months of age without a history of wheeze/asthma)
    - Vote –Yes: 9 and No: 6
  - Children in the age strata 6-23 months, regardless of wheezing history?
    - Vote –Yes: 3 and No: 12
  - Children in the age strata 24-59 months, regardless of wheezing history?
    - Vote –Yes: 15 and No: 0

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Current Status of FluMist Licensure for Young Children

- No FDA decision yet pending resolution of manufacturing issues identified during routine inspection and discussed in May 2007 Warning Letter*
- FDA Warning Letter "not expected to significantly affect availability of FluMist for 2007-2008 influenza season"†
  - MedImmune can continue to manufacture their products while simultaneously making corrective actions
- Delay in BLA supplement decision will require ACIP discussion and vote, and VFC vote, after licensure

***FDA website:** http://www.fda.gov/foi/warning_letters/s6370c.htm

†FDA website: http://www.fda.gov/cber/faq/medimmunega.htm

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Influenza Vaccine Workgroup: Conclusions from FluMist Data Presentations

- Data indicate FluMist efficacy to be non-inferior c/w TIV for children 6 months and older
- Data indicate no safety signal among children 24 months and older without history of wheezing
- Additional information on safety is needed for children 6-23 months old, particularly for children 6-11 months old
  - Wheezing outcomes
  - All-cause hospitalization rates c/w TIV
- Additional information on safety is needed for children ≥24 months old with history of asthma or wheezing

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Influenza Vaccine Workgroup: Planned Discussions after Licensure Decision

- Review FDA-approved age and medical condition indications
- Develop guidance for screening for a history of asthma or recurrent wheezing
- Continue discussions on advantages and disadvantages of recommending LAIV over TIV for healthy young children
- Assess safety analyses from VAERS, VSD, post-licensure studies

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